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National Institute of Neurological Disorders and Stroke

Neural Prosthesis Program



InnerSea Technology

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The goal of the Insulating Biomaterials work is to identify and evaluate materials, coatings, and assembly techniques suitable for protection of integrated circuit devices being considered for neural prosthetic applications.

Instrumentation System

The expanded instrumentation system, shown in Figure 1 has been designed and a first set of boards has been fabricated. The boards have been assembled and are in the electrical de-bug phase. Firmware for the data collection microprocessors must be written before final testing and implementation can be accomplished next quarter. Tube top board design will be finalized next quarter with the possibility of implementing this system on a trial basis in the fall.

The expanded instrumentation system is needed to augment the existing long term soak testing. Plans for testing relatively large sets of devices under least two soak temperatures, and two soak fluid types require additional test capacity. The new system provides many improvements to the old system in terms of reliability, signal integrity, self-test, and “fool-proof” data handling. Notably, all of the high impedance transduction occurs at the input to the electrometer board that plugs into the test tube ID board. Once the currents reach the inputs to the electrometers, they are integrated. The resetting time of the integrator become the signal representation. Thus the output of the electrometer board is a digital signal so the cabling between the test tube and the data collection board is not a factor.

The test tube ID board contains a small memory chip which contains the Identification of the device. This Identification is the name of the device set which is the same identifier used for all lab pages used during construction of the device, all photographs, all data files, and all lab pages associated with analyses. The data collection board then sends the information to the archive computer directly through an Ethernet interface. The archive computer maintains a database of all relevant information to that device. This level of organization is essential for the long term testing program as the number of samples that need



to be tracked over long times, has grown substantially now that more and more devices are surviving saline soak.

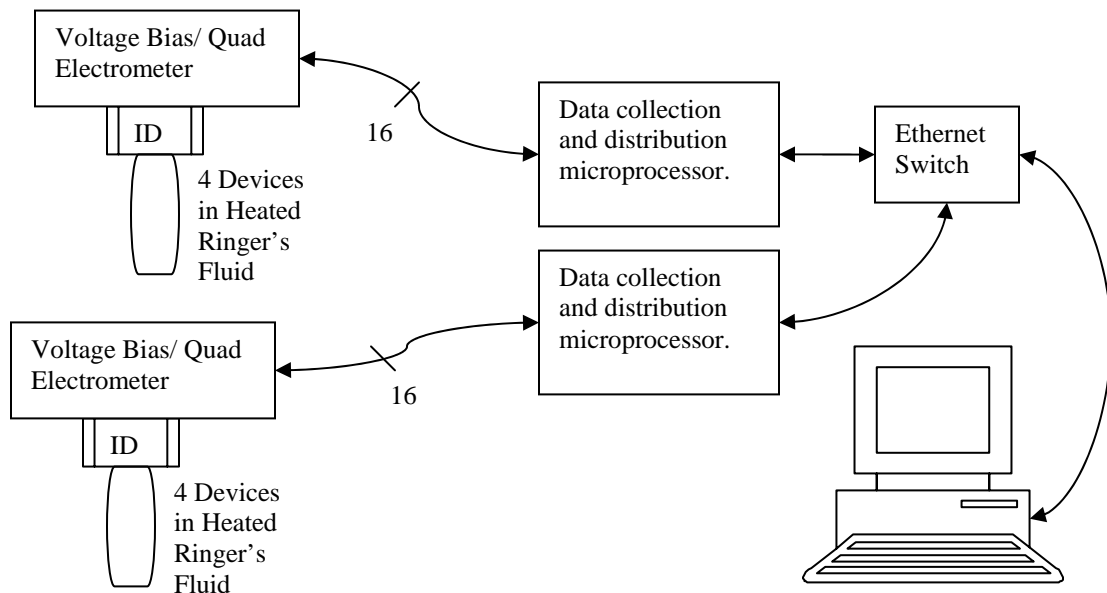


Figure 1: System sketch of instrumentation system.

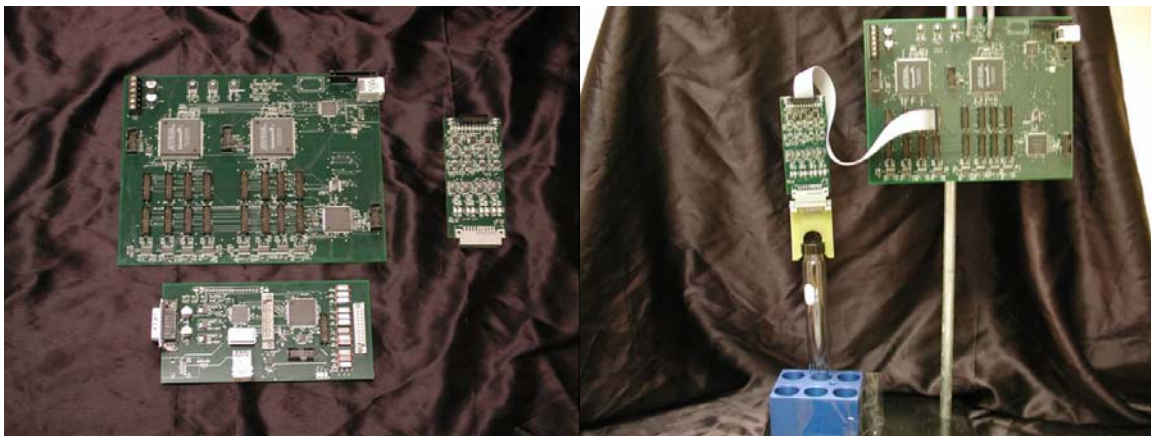


Figure 2: LEFT shows three of the four printed circuit boards fabricated for the long term soak testing system. RIGHT shows a mockup of what the final system configuration will be. See text for details.

Figure 2 LEFT shows the boards that will be the heart of the expanded instrumentation system. The photograph to the left shows the three main boards (tube top board is not yet designed). The small board to right side of the LEFT photo is the electrometer board which will plug into the tube top identification



board as shown in **Figure 2 RIGHT**. The small computer type ribbon cable carries the pulse representation data to the main board. The main board contains the data acquisition circuitry which simply measures the time between pulses from each electrometer and outputs those times, along with the data Identification to the Ethernet interface visible on the upper right corner of the main board. The board shown at the bottom of **Figure 2 LEFT** is the calibration circuit which will be used to calibrate each electrometer array board, and store that calibration information on a small memory chip on that particular electrometer board. Once calibrated, each electrometer board should maintain accuracy indefinitely. Regardless, then which device is plugged into what electrometer array, device ID and calibration will be preserved.

Animal Implant Testing

Device ID	Date Implanted	Date Explanted	Rabbit ID, Description
SCORE	4/12/2001	partial remove 3/10/02, 4/30/04	SCORE, silicon corrosion
PC990106H	8/22/2001	12-Dec-01	PCH, Pass Chip
PC990106I	8/31/2001	17-Sep-02	PCI, Pass Chip
PC990106J	9/19/2001	Nov-01	PCJ, Pass Chip
PC990106K	12/15/2001	5-Jan-03	PCK, Pass Chip
PC990106L	12/27/2001	8-Aug-03	PCL, Pass Chip
RU1	6/6/2002	partial remove 9/10/02, 9/30/03	RU1, preweighed silicone discs
RU2	6/6/2002		RU2, preweighed silicone discs
RBAT1	8/8/2002	12-Jan-03	Simple battery monitor
R1CTB	9/12/2002	14-Apr	1CB, LCP Hybrid Assembly
R1CTC	9/16/2002	Feb-03	1CC, LCP Hybrid Assembly
R1CTD	9/19/2002	Feb-03	1CD, LCP Hybrid Assembly
R1CTE	9/26/2002	2/24/2003	1CE, LCP Hybrid Assembly
R1CTF	10/3/2002	1/21/2003	1CF, LCP Hybrid Assembly
R1CTG	10/3/2002	1/21/2003	1CG, LCP Hybrid Assembly
R1CTH	10/9/2002	14-Apr-03	1CH, LCP Hybrid Assembly
BATMON020718L	10/8/2003		BATL, Battery Monitor
TELE020718A	10/29/2003	Nov 19, 2003 – Bat/cont soak	IDE1, InterDigitated elec on LCP
TELE020718B	11/3/2003	April 16, 2004 – Bat/cont soak	IDE2, InterDigitated elec on LCP
TELE020718C	11/3/2003	April 16, 2004 cracked trace	IDE3, InterDigitated elec on LCP
BSA030131C	12/29/2003		BSC, Biosignal Amp
BSA030131E	3/10/2004	May 7, 2004 Flux/cont soak	BSE, Biosignal Amp
TEMMON020718D	3/12/2004		TD, Temperature Monitor

Table 1: Summary of animal implant testing under this contract.



Animal implants so far under this contract are summarized in Table 1. The SCORE samples are silicon corrosion study pieces that are showing remarkably steady etching for N-type and lightly doped P-type at about 18 microns/year. RU1 and RU2 are uptake study rabbits with disc implants that are periodically removed and weighed to document biochemical uptake by implanted silicones.

PC samples are PassChip implant described in earlier progress reports. These chips functioned perfectly until support circuitry failed due to:

- 1) Flux contamination (mostly from use of water and rosin fluxes on the same substrate which left a residue that was not visible and that the cleaning sequences could not resolve).
- 2) Fiberglass reinforced insulation broke due to implanting wires along the neck which were apparently under great stresses after encapsulation by connective tissue contracted.
- 3) Teflon coated power leads shorted together through a virtual space between the Teflon and silicone when a defect in the silicone was encountered.
- 4) Crack in battery encapsulation caused by apparent weakness in silicone after stresses from removal from mold.
- 5) Lifted wire bond due to apparent deformation of silicone from connective tissue encapsulation and motion caused by battery lead wires.
- 6) Thin silicone over bond wire had an apparent pinhole that caused gold electrolysis and power failure.

While these may seem as obvious failure points, all were not apparent during fabrication nor during soak test prior to implantation:

- 1) The pre-implantation soak time should be longer to catch some of these.
- 2) Only using one type of water soluble flux.
- 3) Cleaning of flux at intermediate stages for easier removal.
- 4) Procured a robotic grade wire with silicone insulation to avoid power supply lead failure.
- 5) Added a fiberglass tape removal assist for the mold.
- 6) Added a strain relief design for the battery leads at the skull to minimize passing stresses to the PassChip bond wires.
- 7) Fabricated a small LCP ribbon connector to carry power and signals to and from the pass chip from the strain relief.
- 8) Developed a stiffness enhanced silicone with similar chemistry to those under test and compatible with them (still under initial testing) to protect wire bonds from small tensile forces (grams) that could lift bonds or break lead wires.



- 9) Noted that odd color of silicones on explant has been caused by Betadine contact prior to implantation – effect on devices unknown but procedures have been modified.

The great news was that the PassChips themselves, with gold on aluminum wire bonds showed no evidence of failure though all the tests were relatively of short duration.

In order to develop the above list of modifications, and test them with real devices but devices that were much less involved than PassChips, a variety of LCP based hybrid circuits were developed and implemented. These were relatively inexpensive to fabricate, would provide detailed test data of the LCP silicone system itself under implant conditions, and not only would facilitate future testing if it all worked out, but might become a substrate of choice for hybrid assemblies that will undoubtedly be necessary for all chronic micromachined neural implants for the foreseeable future.

The next burst of implants came in late summer/fall of 2002 to test the LCP hybrid circuits. While substantial improvements in functional lifetime were realized, there were still issues with flux cleaning and wiring. Even though silicone wiring was in use, and the joints were overcoated with silicone, the silicone-silicone seals failed when implanted, presumably because of small stresses on the seals. This was unexpected or we wouldn't have implanted the devices. The metallization used on the LCP fabrications could not withstand the heat cycling and bending inherent in the assembly and implant process so several devices failed before resorting to a stainless steel backing plate and also strain relieving the battery supply wires more thoroughly.

With these findings, a new set of implants was developed. A search for better encapsulants for these silicone wire coatings silicones was not successful, so the wires are now completely overcoated with the encapsulation to avoid the issue for now. Instead of using two batteries to achieve the 5 volt bias usually used, a single battery was used which provided 3.6 volt supply to a 2.5 volt regulator. The single battery fit nicely behind the skull just below the ears in a small hollow, and leads could be tunneled under the superficial muscles to lie directly on the skull. Thus the macro-motions were eliminated. Another means of providing the higher voltage will be developed once these are working well.

An optical telemetry battery monitor, produced with an LCP substrate has functioned perfectly since October 8, 2003, and is still under test in a rabbit. Measurements are taken periodically using a high speed optical pulse detector developed for that purpose. For this implant, the pulse rate is inversely proportional to battery voltage. The circuit operates on a few microamperes and so should remain functional for 5-10 years on the implanted lithium battery.

Of three LCP IDE testers, two failed due to battery encapsulation issues. Likely, the fiberglass tape used to extract the batteries provided a pathway for saline intrusion onto the battery casing. Sometimes, probably when the silicone had been overstressed and moved relative to the case, the saline could infiltrate to the battery terminals causing rapid discharge and implant failure. Also, a British



study was recently found that indicated that isopropyl alcohol attacks silicones which may have been responsible for some of these failures as we replace Betadine with isopropyl. More will be done to clarify this before new implants.

third failed due to a cracked trace which was unfortunate. This was likely a problem during the assembly, but it was not expressed until the device was implanted and perhaps bent just in the right way to cause failure. The two battery failures were explanted and the batteries replaced. These are now soaking at 37°C in saline and functioning perfectly, measuring surface resistivity on the order of 1e12ohms.

One recent device (biosignal amplifier example) failed due to a flux corrosion problem once again. We're not sure how this happened, but it was probably due to an assembly error.

Another biosignal amplifier is functioning perfectly. This LCP based hybrid circuit encodes EMG or other biosignals, and uses our optical telemetry to send data at a 4kHz base rate. This device draws about 12μA of current and thus may only last 3 years or so. A temperature monitor is functioning perfectly. This device has a low data rate and thus should last close to 10 years.

Now we feel we are close to being able to produce a PassChip implant once again to monitor CMOS function in a subdural environment. One remaining issue is how best to protect the wire bonds. This will be addressed next quarter.

Peel Testing

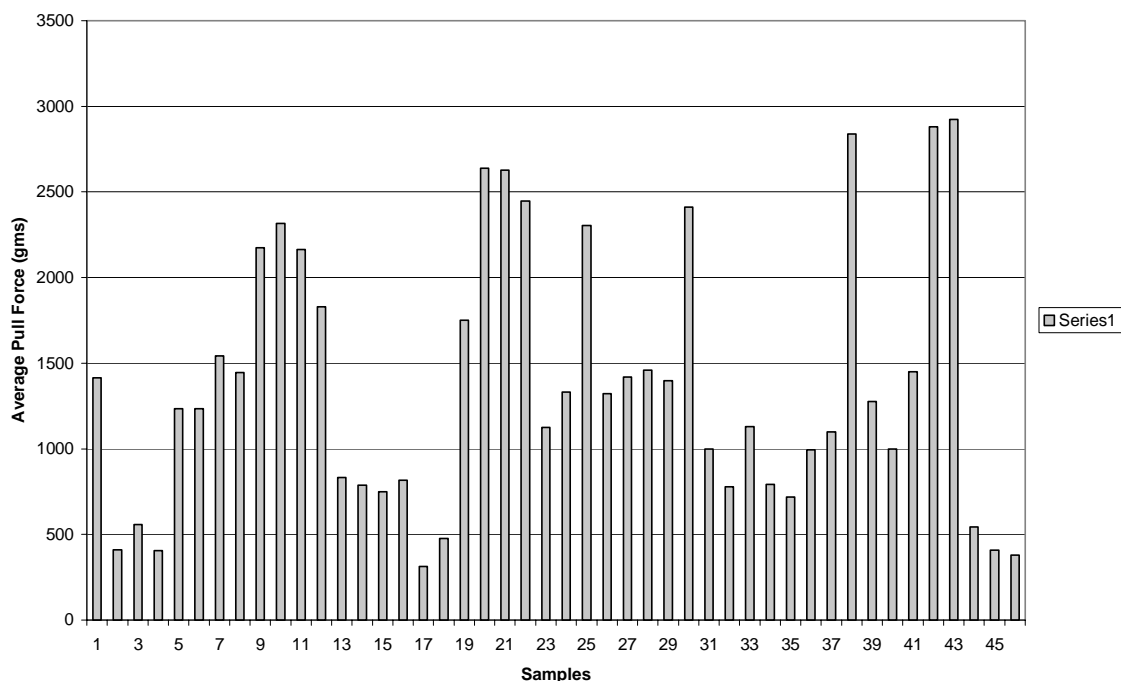


Figure 3: Summary of MED4-4220 peel testing results during the past two years of identifying the basis for such extreme variation in what would be expected to be a routine, robust measurement.



Experiments with use of peel testing continued in an effort to clarify the wide variations observed in what would normally be expected to yield repeatable, robust results. The original rationale for developing the peel test was to be able to rapidly screen encapsulants, contamination procedures, and cleaning procedures without the expense of assembling the triple track devices. The assumption behind the use of the peel test is that if the bond between the encapsulant and surface being protected weakens over time, then the candidate encapsulant is probably not a good choice for long term protection of an implantable integrated circuit. Since the force of adhesion necessarily must depend on both the density of bonds, and the strength of the bonds, it seems obvious that this would be an excellent measure.

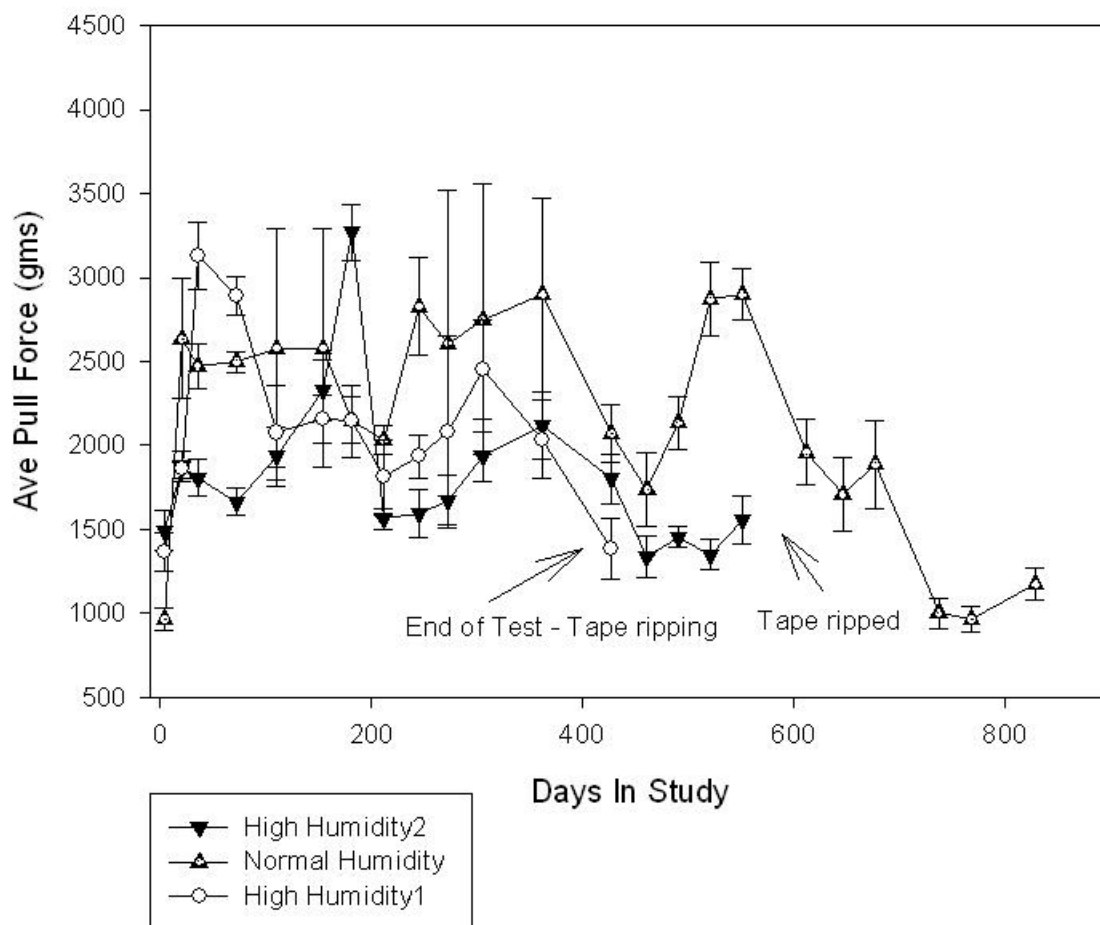


Figure 4: Results of peel testing of samples cured under normal humidity or high (saturated) humidity conditions.



However, the results obtained were highly variable as shown in Figure 3. Many variations in assembly techniques were tried, but none appeared to be correlated with bond strength with the possible exception of cure temperature, though this isn't yet fully clarified. Humidity and surface hydration were obvious variables for silicone bonding since it is generally accepted that the mechanism for silicone bonding to silica surfaces was through a hydroxyl intermediary [1]. Since humidity varies widely over the course of a year in the Northeast, it seemed reasonable to look at humidity as a factor, along with varying cleaning procedures to enhance or reduce hydroxylation of the surface. Results of the humidity study are shown in Figure 4 which little if any dependence on humidity compared to the variations shown in Figure 3.

The stronger correlation, in looking back through the data, may have been due to micro-bubbles. When encapsulant mixtures were allowed to de-air longer, or were vacuum de-aired, or were centrifuged (which also removes air), force of adhesion generally exceeded the strength of the material.

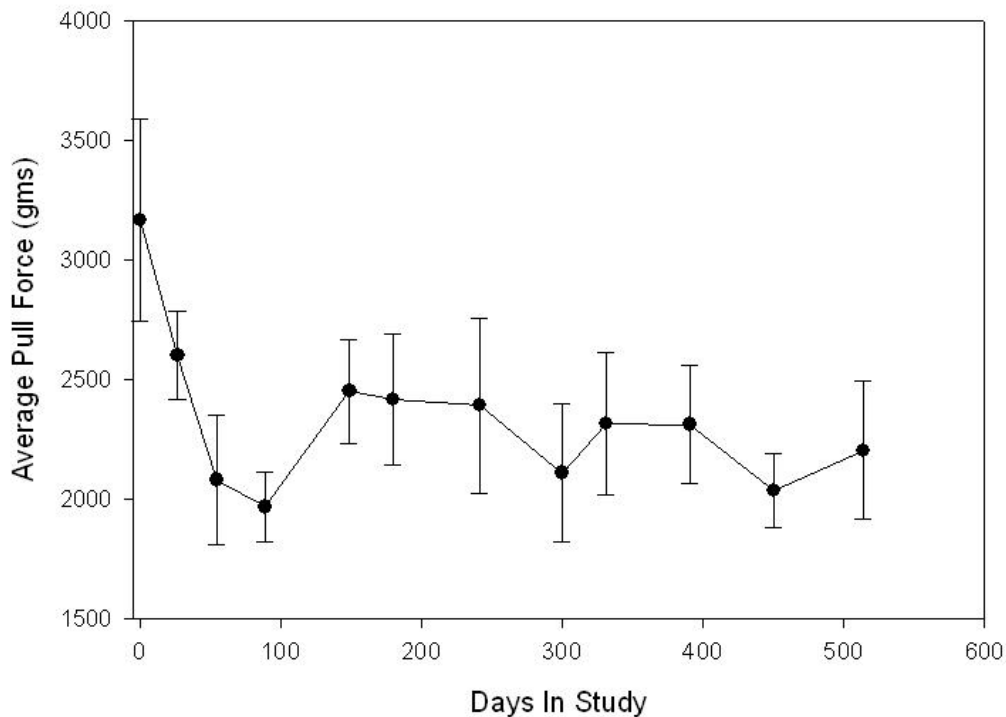


Figure 5: MED-2000 acetoxycure silicone peel test (37°C Saline, pre-release strip era).



In spite of this variability, these tests are still quite useful. An example is that we are now beginning to look at silicone cure systems other than 2 part platinum catalyzed. Another well developed class of silicones is the acetoxy cure system. These silicones cure at room temperature in the presence of water vapor. The cure reaction results in release of acetic acid vapor. Acetoxy cure materials are generally known to exhibit superior adhesion on glass. Acetoxy cure materials are also widely used to adhere silicones to silicones which will be helpful in sealing the silicone insulated lead wires on battery powered assemblies.

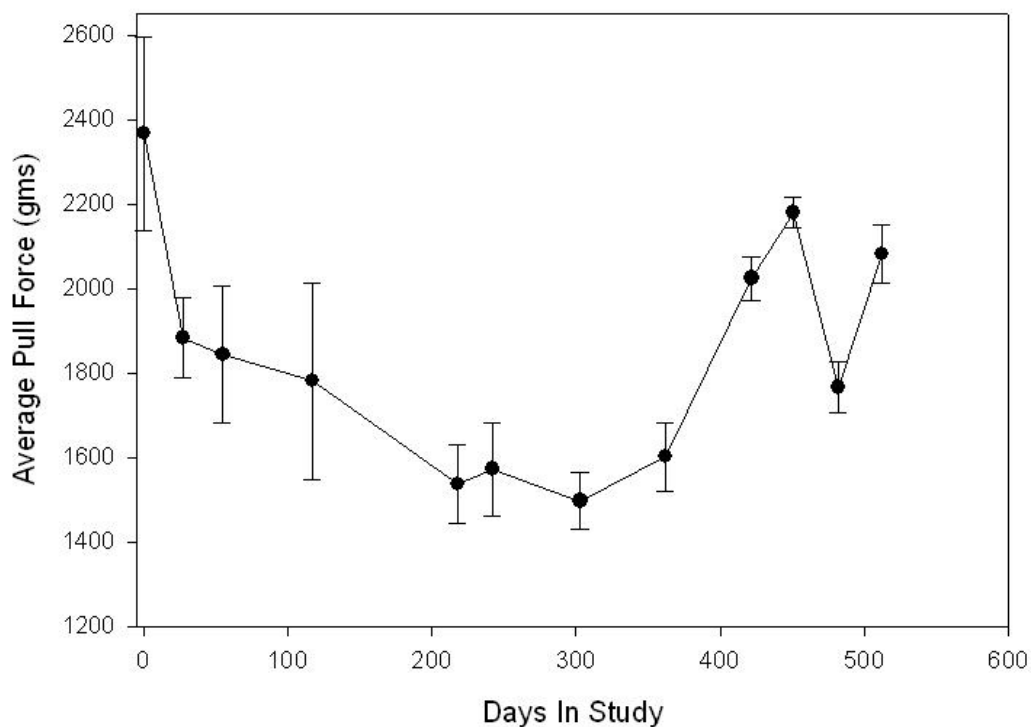


Figure 6: MED-1511 acetoxy cure silicone peel test (37°C Saline, pre-release strip era)

Two example acetoxy cure materials with different flow properties were procured from Nusil – MED-1511, and MED-2000. Both are unrestricted silicones, so they have FDA approval for long term implantation. Figure 5 and Figure 6 show results from long term peel testing of these acetoxy cure materials. Both exhibit apparently stronger adhesion and bulk strength properties than the 2 part platinum catalyzed materials studied thus far. New samples, using Kapton release stripes will be implemented to verify these results. Triple track devices



on quartz and LCP will also be fabricated and placed under test in view of these promising results.

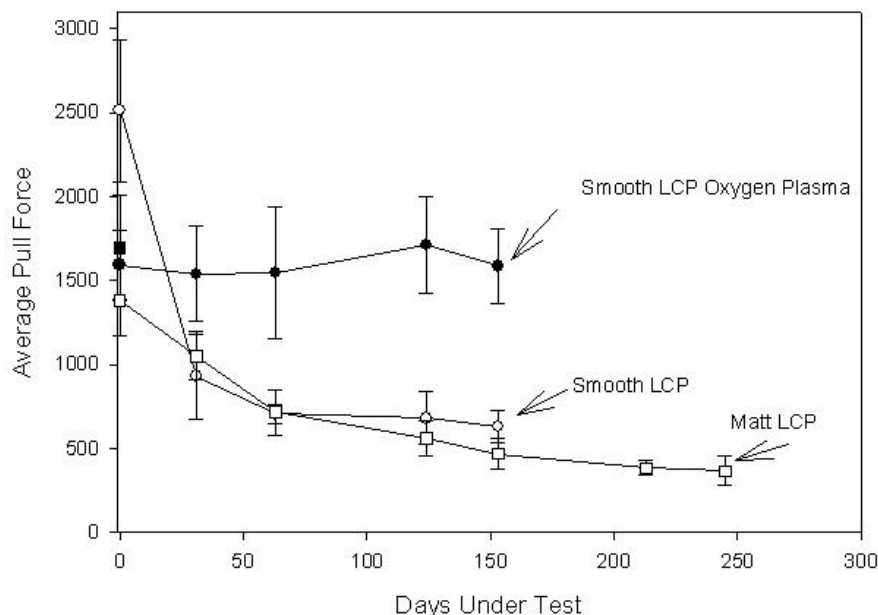


Figure 7: Peel test results of MED4-4220 on LCP substrates (37°C Saline, pre-release strip era) showing positive, long lasting effect of oxygen plasma on LCP-silicone adhesion.

LCP (Liquid Crystal Polymer) substrates have been under test for several years thus far and in all cases so far have shown great promise as a photolithographically stable material that is thin, flexible, biocompatible, and bioresistant. Triple track devices have also shown good results when there are no defects at time of assembly. However, such testing is quite slow and laborious to work through all the variables of interest (cleaning, contamination, cure cycles, encapsulant variations). Accordingly, peel test samples were assembled with two types of LCP (Matt finish and Smooth), and subjected to either an oxygen plasma clean or a standard solvent sequence clean. One sample (oxygen plasma on Matt finish) failed when the LCP peeled from the underlying support substrate and could not be tested. The results of the other three are shown in

Figure 7. The improvement in adhesion for the oxygen plasma treated LCP substrates is quite impressive, though these results need to be repeated as peel tests, and will also now be repeated with triple track devices.

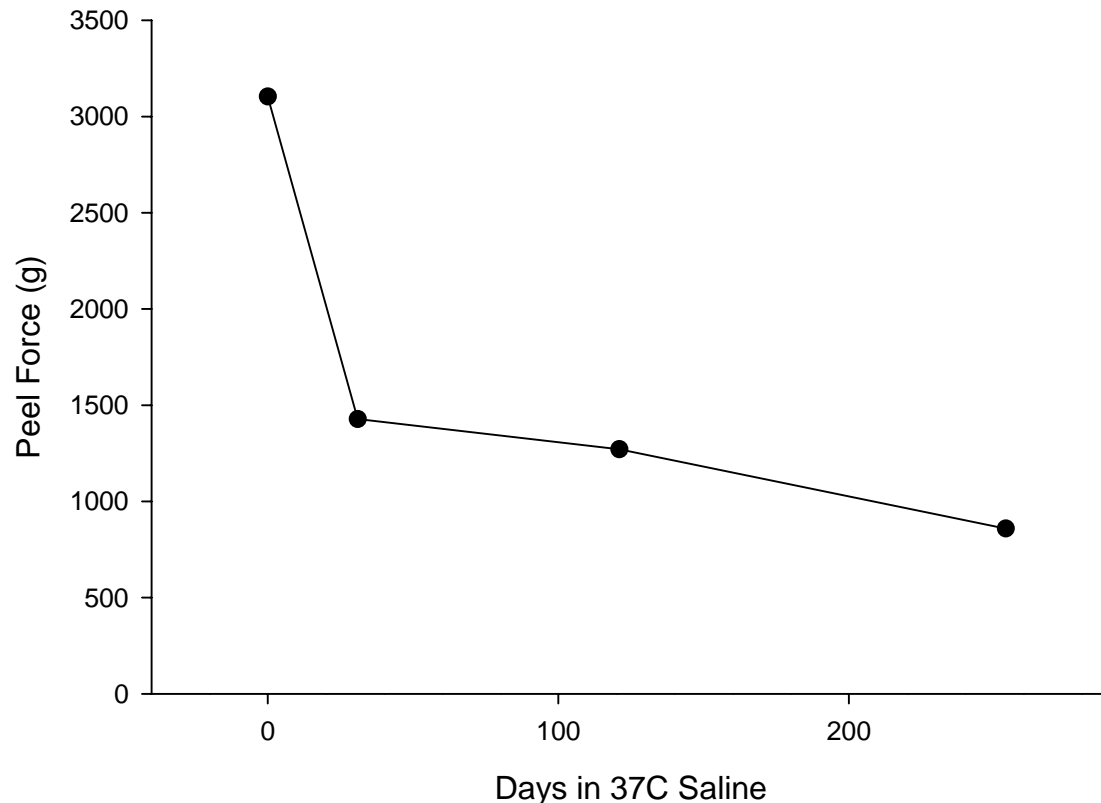


Figure 8: Peak peel force results from MED4-4220 on a slide with Kapton release stripes in place. Results show a monotonicity which is refreshing for peel data that we have gathered.

To summarize the peel test data thus far, a number of variables have been investigated to ensure that all that can be controlled, and that are of significance are being controlled. Use of Kapton release tape stripes as previously reported, has resulted in cleaner data since the pull always begins at a well defined release edge. Recent data of a Kapton peel test for MED4-4220 is shown in Figure 8. The data is monotonic which is a refreshing change from prior results without the Kapton release stripes. While the peel test is limited to samples that fail at peel forces below the breakstrength of the material, they still indicate adhesion below that level, and also changes in adhesion as well as changes in mechanical strength.

Since peel test samples are relatively easy to prepare, can be followed for several years or more if multiple samples are created in the beginning, and are now producing reliable, consistent results, they will be continued and used to pre-screen promising materials prior to investing in the long term soak testing. The most obvious application at the present time is to sort through the large variety of



adhesion promoters, all of which have as chemical basis for potentially improving adhesion, but it is not known if that will occur under long term soak conditions.

HFCVD of Silicones

“Tweaking” of the tert-butyl peroxide catalyzed vapor phase hot filament silicone deposition from V_3D_3 was continued in an effort to improve the deposition rate. Samples of the films were assembled into saline soak tubes using the standard “O-ring” assembly that exposes the front-side of coated silicon squares to biased saline soak. These devices have only recently been placed under test, but are exhibiting very high initial resistances, most greater than $1e12$ which is quite good for a silicone, especially a thin-film silicone! Appended is a paper, partially supported by this contract, submitted to Langmuir journal covering the grafting of biomolecules to silicones to promote surface functionality [2].

Literature Cited:

1. Noll, W., *Chemistry and Technology of Silicones*. 2nd ed. 1968, New York: Academic Press.
2. Murthy, S., B. Olsen, and K. Gleason, *Peptide attachment to vapor deposited polymeric thin films*. Langmuir, 2004. **20**: p. 4774-4776.